

We claim:

1. A method for making a hypermutated antigen, comprising introducing into a mammalian cell that expresses a preselected antigen a polynucleotide comprising a dominant negative allele of a mismatch repair gene.
2. The method of claim 1 wherein the polynucleotide is introduced by transfection of a suspension of cells *in vitro*.
3. The method of claim 1 wherein the mismatch repair gene is *PMS2*.
4. The method of claim 1 wherein the mismatch repair gene is human *PMS2*.
5. The method of claim 1 wherein the mismatch repair gene is *MLH1*.
6. The method of claim 1 wherein the mismatch repair gene is *PMS1*.
7. The method of claim 1 wherein the mismatch repair gene is *MSH2*.
8. The method of claim 1 wherein the mismatch repair gene is *MSH2*.
9. The method of claim 4 wherein the allele comprises a truncation mutation.
10. The method of claim 4 wherein the allele comprises a truncation mutation at codon 134.
11. The method of claim 10 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2*.
12. The method of claim 1 wherein the polynucleotide is introduced into a fertilized egg of an animal.
13. The method of claim 12 wherein the fertilized egg is subsequently implanted into a pseudo-pregnant female whereby the fertilized egg develops into a mature transgenic animal.
14. The method of claim 12 wherein the mismatch repair gene is *PMS2*.
15. The method of claim 12 wherein the mismatch repair gene is human *PMS2*.
16. The method of claim 12 wherein the mismatch repair gene is human *MLH1*.
17. The method of claim 12 wherein the mismatch repair gene is human *PMS1*.
18. The method of claim 11 wherein the mismatch repair gene is human a human mutL homolog.

19. The method of claim 15 wherein the allele comprises a truncation mutation.
20. The method of claim 15 wherein the allele comprises a truncation mutation at codon 134.
21. The method of claim 19 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2*.
22. A homogeneous composition of cultured, hypermutable, mammalian cells which comprise a preselected antigen and a dominant negative allele of a mismatch repair gene.
23. The isolated hypermutable cell of claim 22 wherein the mismatch repair gene is *PMS2*.
24. The isolated hypermutable cell of claim 23 wherein the mismatch repair gene is human *PMS2*.
25. The isolated hypermutable cell of claim 22 wherein the mismatch repair gene is *MLH1*.
26. The isolated hypermutable cell of claim 22 wherein the mismatch repair gene is *PMS1*.
27. The isolated hypermutable cell of claim 22 wherein the mismatch repair gene is a human *mutL* homolog.
28. The isolated hypermutable cell of claim 22 wherein the cells express a protein consisting of the first 133 amino acids of hPMS2.
29. A method for generating a mutation in a gene encoding an antigen of interest comprising
 - growing a mammalian cell comprising said gene encoding an antigen of interest and a dominant negative allele of a mismatch repair gene, and
 - determining whether said gene encoding an antigen of interest harbors a mutation.
30. The method of claim 29 wherein determining whether said gene encoding an antigen of interest harbors a mutation is accomplished by analyzing the nucleotide sequence of said gene.
31. The method of claim 30 wherein said nucleotide sequence is an mRNA transcribed from said gene.

32. The method of claim 29 wherein determining whether said gene encoding an antigen of interest harbors a mutation is accomplished by analyzing a protein encoded by said gene.
33. The method of claim 30 wherein determining whether said gene encoding an antigen of interest harbors a mutation is accomplished by analyzing the phenotype of said gene.
34. The method of claim 32 wherein analyzing of said protein comprises analyzing the antigenicity and immunogenicity of said protein.
35. A method for generating a mutation in a gene encoding an antigen of interest comprising
 - growing a cell comprising said gene and a polynucleotide encoding a dominant negative allele of a mismatch repair gene; and
 - testing the cell to determine whether the cell harbors a mutation in said gene yielding at least one new biochemical feature of said antigen.
36. The method of claim 35 wherein said new biochemical feature is selected from the group consisting of increased antigenicity and increased immunogenicity.
37. The method of claim 35 wherein said testing comprises analyzing primary structure of said gene.
38. The method of claim 35 wherein said testing comprises analyzing the secondary structure of said gene.
39. The method of claim 35 wherein said testing comprises analyzing the antigenicity and immunogenicity of the polypeptide encoded by said gene.
40. The method of claim 1 wherein said introduction of said polynucleotide is in the presence of at least one DNA mutagen.
41. The method of claim 35 wherein said testing comprises analyzing a nucleotide sequence said gene.
42. The method of claim 35 wherein said testing comprises analyzing mRNA transcribed from said gene.

43. The method of claim 35 wherein said testing comprises analyzing the antigen protein encoded by the gene of interest.
44. The method of claim 35 wherein said testing comprises analyzing the biochemical activity of the protein encoded by said gene.
45. A hypermutable transgenic mammalian cell made by the method of claim 35.
46. The transgenic mammalian cell of claim 45 wherein the cell is from primate.
47. The transgenic mammalian cell of claim 45 wherein the cell is from rodent.
48. The transgenic mammalian cell of claim 45 wherein the cell is from human.
49. The transgenic mammalian cell of claim 45 wherein the cell is eucaryotic.
50. The transgenic mammalian cell of claim 45 wherein the cell is prokaryotic.
51. A method for making randomly altered forms of a secreted antigen comprising introducing a polynucleotide encoding a tagged antigen into an MMR defective cell.
52. The method of claim 51 wherein said tagged antigen is screened for increased antigenicity.
53. The method of claim 51 wherein said tagged antigen is screened for increased immunogenicity.
54. The method of claim 51 wherein the cells are made MMR defective by introducing at least one dominant negative allele of an MMR gene.
55. The method of claim 51 wherein the cells are naturally MMR defective.
56. A method of producing a mutated antigen in a reversibly unstable cell comprising introducing into a cell containing a preselected antigen of interest, an inducible expression vector comprising a polynucleotide encoding a dominant negative allele of a mismatch repair gene; inducing said cell to express said dominant negative mismatch repair gene; and detecting at least one new biochemical feature of said antigen.
57. The method of claim 56 wherein said new biochemical feature is selected from the group consisting of a nucleotide mutation, increased antigenicity and increased immunogenicity.
58. The method of claim 56 wherein said preselected antigen of interest is encoded on a polynucleotide previously transfected into said cell.

59. The method of claim 56 further comprising ceasing induction of said dominant negative allele of a mismatch repair gene, thereby stabilizing said cell.
60. The method of claim 58 further comprising isolating the polynucleotide previously transfected into said cell after detection of said new biochemical feature.
61. An polynucleotide molecule for expressing an antigen in a hypermutable cell comprising an expression cassette wherein said cassette comprises a 3' sequence encoding a plurality of histidine residues, a 5' leader sequence of an expressed gene, and a polylinker to allow cloning of a nucleotide sequence encoding a preselected antigen.
62. The polynucleotide molecule of claim 61 wherein said cell is a mammalian cell.
63. The polynucleotide molecule of claim 61 wherein said cell is a human cell.
64. The method of claim 63 wherein said 5' leader sequence is a 5' leader sequence of IL-2.
65. A method of producing a mutated antigen comprising introducing a polynucleotide encoding a preselected antigen in the expression cassette said polynucleotide molecule of claim 61, and introducing said polynucleotide molecule into a cell comprising a dominant negative allele of a mismatch repair gene.
66. A hypermutated antigen produced by the method of claim 65.
67. A method of eliciting an immune response in an animal comprising administering to said animal an immunogenic amount of at least one hypermutated antigen of claim 66.
68. The method of claim 67 wherein said antigen is a mutated form of an antigen derived from a pathogenic organism selected from the group consisting of, bacteria, fungi, protozoa, helminths, and viruses.
69. An immunogenic composition comprising at least one hypermutated antigen of claim 66 and a pharmaceutically acceptable carrier.